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Effect of continuous positive airway pressure on insulin growth factor-1 in patients with obstructive sleep apnea: A meta-analysis

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ABSTRACT

Objective: Obstructive sleep apnea (OSA) has been recognized as being associated with low level of insulin growth factor-1 (IGF-1). However, the impact of OSA treatment using continuous positive airway pressure (CPAP) on IGF-1 remains controversial. We performed a meta-analysis to determine whether effective CPAP therapy could increase IGF-1 levels.

Design: Two reviewers independently searched PubMed, Cochrane library, Embase and Web of Science before September 2014. Information on characteristics of subjects, study design and pre- and post-CPAP treatment of serum IGF-1 was extracted for analysis. Standardized mean difference (SMD) was used to analyze the summary estimates for CPAP therapy.

Results: Six articles with 168 patients were included in this meta-analysis, including five observational studies and one randomized controlled study. The meta-analysis showed that CPAP was associated with a statistically significant increase in IGF-1 in OSA patients (SMD = −0.436, 95% confidence interval = −0.653 to −0.218, $P = 0.000$).

Conclusions: This meta-analysis suggested that CPAP therapy was associated with an increase in IGF-1 in patients with OSA. Further large-scale, well-designed interventional investigations are needed to clarify this issue.

1. Introduction

Obstructive sleep apnea (OSA) is a common medical condition characterized by repetitive partial or complete obstruction of the upper airway [1]. The prevalence of OSA is estimated to be 2% to 4% in the general population and 35% to 45% in obese individuals [2,3]. The repetitive episodes of upper-airway obstruction in sleep apnea are often associated with repetitive nocturnal oxygen desaturation and arousals that disrupt sleep architecture and reduce slow-wave sleep, both of which could affect the sleep-entrained or diurnal rhythms of pituitary-dependent hormones [4].

Insulin growth factor-1 (IGF-1) is a 7.7-kDa single-chain polypeptide of 70 amino acids that is similar in sequence to proinsulin [5]. Growth hormone (GH) stimulates the synthesis of IGF-1 in the liver and regulates the paracrine production of IGF-1 in many other tissues. IGF-1 is considered to be an important growth factor, mediating the anabolic and linear growth promoting effect of pituitary GH protein [6]. An accumulating body of evidence showed that OSA was associated with significant decrease in serum IGF-1 [7–9].

An effective noninvasive treatment for OSA has become available and continuous positive airway pressure (CPAP) may eliminate hypoxic episodes and result in improved sleep. However, a number of studies [8,10–15] have yielded conflicting results regarding the impact of CPAP therapy on IGF-1 levels in OSA patients, among those most studies with small sample size, which have not enough statistical power to address this issue adequately and effectively. In this study, a meta-analysis was conducted to quantitatively evaluate the impact of CPAP on IGF-1 levels in OSA patients.

2. Methods

2.1. Search strategy

We searched PubMed, Web of Science, Cochrane Library and Embase before September 2, 2014, on original English language studies, using the following search terms(continuous positive airway pressure or CPAP) and (sleep apnea or sleep apnoea) combined with (insulin growth factor-1 or IGF-1 or somatomedin C). In addition, the reference lists of relevant publications were manually searched for related studies. Two independent assessors identified relevant studies based on title and abstract that included empirical data related to the treatment effect on IGF-1 in OSA.

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2.2. Inclusion/exclusion criteria of literature

Studies were included if they met the following criteria: (1) All subjects of the study were limited to adults(age > 18) with newly diagnosed OSA. (2) The intervention was an application of CPAP. (3) The study must have both before and after CPAP IGF-1 values reported. (4) CPAP had to be used for ≥ 4 weeks before and after repeat IGF-1. (5) The study provided sufficient data that allowed for a meta-analysis. When multiple studies reported outcomes using the same patient group, the study with the largest population was included.

Excluded criteria were as follows: (1) studies that did not satisfy the inclusion criteria would be excluded; (2)non-English article; (3) abstracts, case reports, editorials, expert opinions, letters, animal studies and reviews without original data; and (4)unpublished data from conference. If the required data of studies was ambiguous, the corresponding author was contacted; after two no-response attempts, the studies were also ruled out. Any disagreement between the two reviewers was resolved by discussing with a third reviewer.

2.3. Data extraction

Data were extracted from each study by a single author and then reviewed by a second author to ensure that no errors were made. The following variables were extracted from each study: first author, publication year, country of the study, sample size, patient inclusion criteria, participant characteristics, study design, mean daily CPAP usage time, duration of CPAP therapy, serum IGF-1 levels before and after CPAP treatment.

2.4. Statistical analysis

The meta-analysis was conducted using Stata statistical software(Version 12.0, Stata Corporation). Considering IGF-1 measured and reported differently, standardized mean difference (SMD) was used for analyzing the summary estimates. Q and I^2 statistics were used to determine statistical heterogeneity among individual studies [16]. Heterogeneity was considered to be significant at $p < 0.10$ for the Q statistic [17]. An I^2 greater than 50% was considered substantial heterogeneity in this meta-analysis. Random-effects model was performed to combine effect size if significant heterogeneity was observed; otherwise, fix effects model was conducted. Sensitivity analysis was conducted to investigate the influence of a single study on overall efficacy of CPAP. Publication bias was presented using funnel plot and tested by "Begg test" and "Egger test." A $p < 0.05$ was adopted as statistical significance.

3. Results

3.1. Searching results

A total of 39 studies were retrieved to screen after searching duplication. After review of the titles and abstracts, 27 studies were excluded whereas 12 were considered to be potentially relevant. Of the 12 studies, 6 were excluded from the sample for the following reasons: 1 was conference article [18], 2 lacked essential data [19,20], the data of one study presented as bar graph [21], one study had no measure unit of essential data [22] and one study in which therapy duration <4 weeks [23]. The detailed steps of the literature search were shown in Fig. 1.

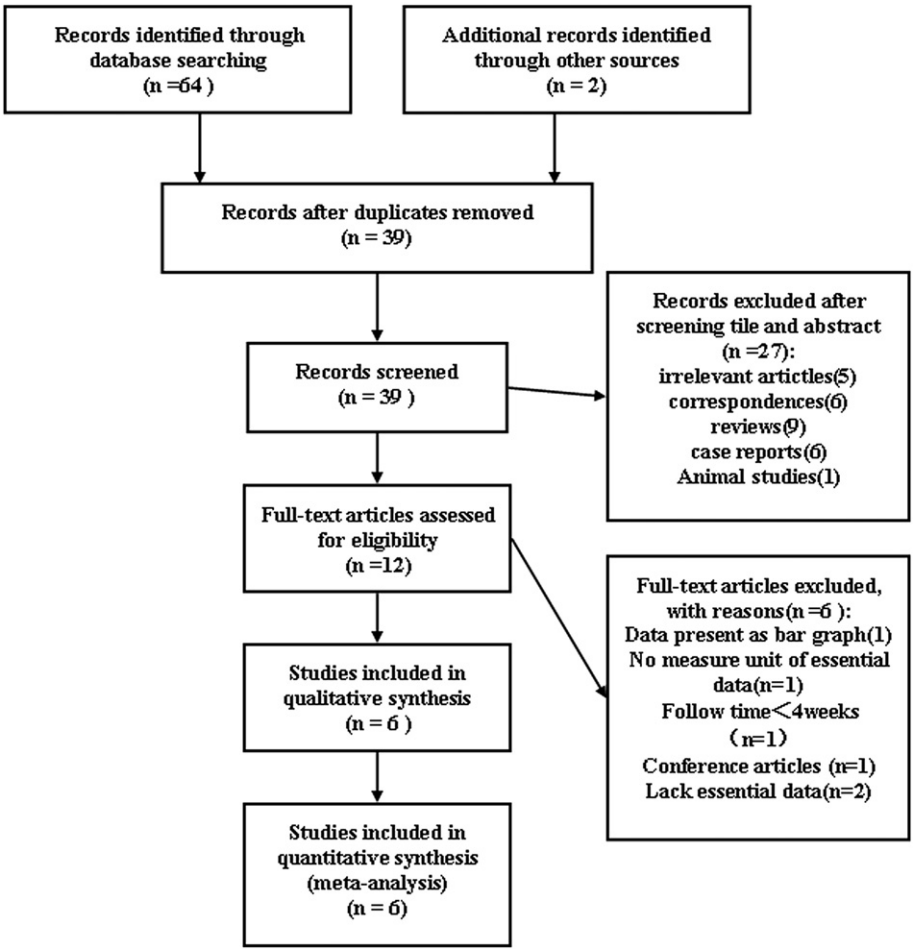

Fig. 1. Flow diagram of study selection.